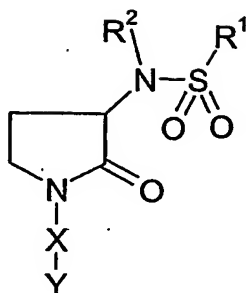


Claims

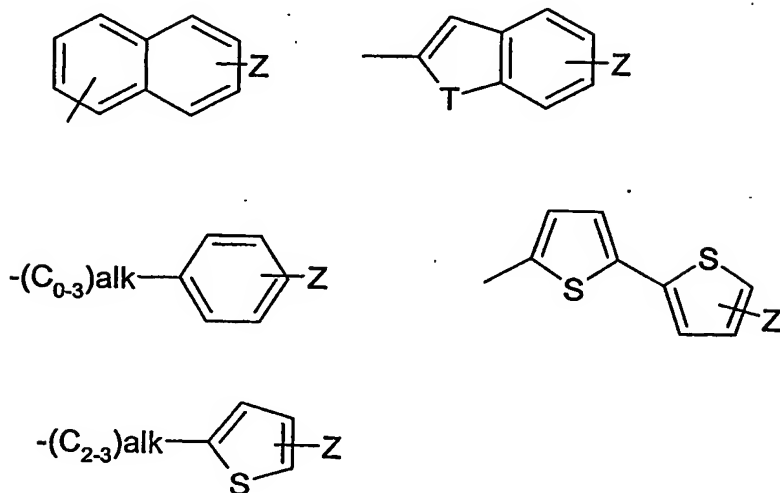
1. A compound of formula (I):



(I)

wherein:

R¹ represents a group selected from:



each ring of which optionally contains a further heteroatom N,

10 Z represents an optional substituent halogen,

alk represents alkylene or alkenylene,

T represents S, O or NH;

R² represents hydrogen, -C₁₋₆alkyl, -C₁₋₃alkylCONRᵃRᵇ, -C₁₋₃alkylCO₂C₁₋₄alkyl, -CO₂C₁-  
15 4alkyl or -C₁₋₃alkylCO₂H;

Rᵃ and Rᵇ independently represent hydrogen, -C₁₋₆alkyl, or together with the N atom to which they are bonded form a 5-, 6- or 7- membered non-aromatic heterocyclic ring

optionally containing an additional heteroatom selected from O, N or S, optionally substituted by  $C_{1-4}$ alkyl, and optionally the S heteroatom is substituted by O, i.e. represents  $S(O)_n$ ;

5 n represents 0-2;

X represents phenyl or a 5- or 6- membered aromatic heterocyclic group containing at least one heteroatom selected from O, N or S, each of which is optionally substituted by 0-2 groups selected from: halogen,  $-C_{1-4}$ alkyl,  $-C_{2-4}$ alkenyl,  $-CN$ ,  $-CF_3$ ,  $-NR^aR^b$ ,  $-C_{0-4}$ alkylOR<sup>e</sup>,  
10  $-C(O)R^f$  and  $-C(O)NR^aR^b$ ;

R<sup>e</sup> represents hydrogen or  $-C_{1-6}$ alkyl;

R<sup>f</sup> represents  $-C_{1-6}$ alkyl;

15

Y represents a group  $-C(R^x)(R^z)C_{0-2}$ alkylNR<sup>c</sup>R<sup>d</sup>;

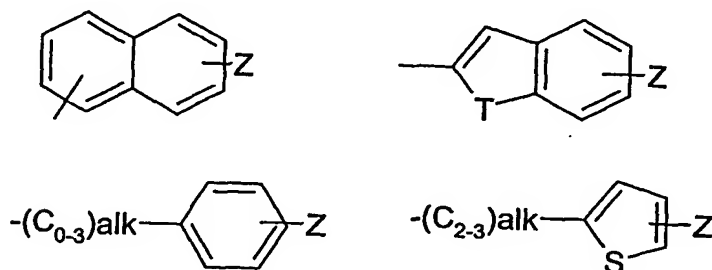
R<sup>x</sup> represents  $C_{1-4}$ alkyl optionally substituted by halogen;

20 R<sup>z</sup> represents hydrogen or  $C_{1-4}$ alkyl optionally substituted by halogen;

R<sup>c</sup> and R<sup>d</sup> independently represent hydrogen,  $-C_{1-6}$ alkyl,  $-C_{1-4}$ alkylOH, or together with the N atom to which they are bonded form a 4-, 5-, 6- or 7- membered non-aromatic heterocyclic ring, the 5-, 6- or 7- membered non-aromatic heterocyclic ring optionally  
25 containing an additional heteroatom selected from O, N or S, optionally substituted by  $C_{1-4}$ alkyl;  
and/or pharmaceutically acceptable derivative thereof.

2. A compound according to claim 1 wherein R<sup>1</sup> represents a group selected from:

30



each ring of which optionally contains a further heteroatom N,  
Z represents an optional substituent halogen,

alk represents alkylene or alkenylene,

T represents S, O or NH

and/or pharmaceutically acceptable derivative thereof.

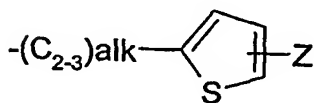
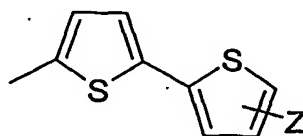
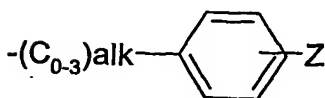
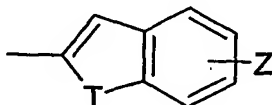
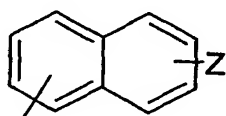
5 3. A compound according to claim 1 or claim 2 wherein  $R^2$  represents hydrogen and/or pharmaceutically acceptable derivative thereof.

4. A compound according to any one of claims 1-3 wherein X represents phenyl or a 5- or 6- membered aromatic heterocyclic group containing at least one heteroatom selected  
10 from O, N or S, each of which is optionally substituted by 0-2 groups selected from: halogen,  $-C_{1-4}$ alkyl and  $-NR^aR^b$  and/or pharmaceutically acceptable derivative thereof.

5. A compound according to any one of claims 1-4 wherein Y represents a group  $-C(R^*)(R^z)NR^cR^d$  and/or pharmaceutically acceptable derivative thereof.

15

6. A compound according to claim 1 wherein  $R^1$  represents a group selected from:



each ring of which optionally contains a further heteroatom N,

Z represents an optional substituent halogen,

alk represents alkylene or alkenylene,

20 T represents S, O or NH;

$R^2$  represents hydrogen,  $-C_{1-6}$ alkyl,  $-C_{1-3}$ alkylCONR<sup>a</sup>R<sup>b</sup>,  $-C_{1-3}$ alkylCO<sub>2</sub>C<sub>1-4</sub>alkyl,  $-CO_2C_{1-4}$ alkyl or  $-C_{1-3}$ alkylCO<sub>2</sub>H;

25 R<sup>a</sup> and R<sup>b</sup> independently represent hydrogen,  $-C_{1-6}$ alkyl, or together with the N atom to which they are bonded form a 5-, 6- or 7- membered non-aromatic heterocyclic ring

optionally containing an additional heteroatom selected from O, N or S, optionally substituted by C<sub>1-4</sub>alkyl, and optionally the S heteroatom is substituted by O, i.e. represents S(O)<sub>n</sub>;

- 5 X represents phenyl or a 5- or 6- membered aromatic heterocyclic group containing at least one heteroatom selected from O, N or S, each of which is optionally substituted by 0-2 groups selected from: halogen, -C<sub>1-4</sub>alkyl, -C<sub>2-4</sub>alkenyl, -CN, -CF<sub>3</sub>, -NR<sup>a</sup>R<sup>b</sup>, -C<sub>0-4</sub>alkylOR<sup>e</sup>, -C(O)R<sup>f</sup> and -C(O)NR<sup>a</sup>R<sup>b</sup>;

- 10 R<sup>e</sup> represents hydrogen or -C<sub>1-6</sub>alkyl;

R<sup>f</sup> represents -C<sub>1-6</sub>alkyl;

Y represents a group -C(R<sup>x</sup>)(R<sup>z</sup>)C<sub>0-2</sub>alkylNR<sup>c</sup>R<sup>d</sup>;

15

R<sup>x</sup> represents C<sub>1-4</sub>alkyl optionally substituted by halogen (e.g. CF<sub>3</sub>, -CH<sub>2</sub>CF<sub>3</sub>);

R<sup>z</sup> represents hydrogen or C<sub>1-4</sub>alkyl optionally substituted by halogen (e.g. CF<sub>3</sub>, -CH<sub>2</sub>CF<sub>3</sub>);

- 20 R<sup>c</sup> and R<sup>d</sup> independently represent hydrogen, -C<sub>1-6</sub>alkyl, -C<sub>1-4</sub>alkylOH, or together with the N atom to which they are bonded form a 5- or 6- membered non-aromatic heterocyclic ring optionally containing an additional heteroatom selected from O, N or S, optionally substituted by C<sub>1-4</sub>alkyl;  
and pharmaceutically acceptable derivatives thereof.

25

7. A compound according to claim 1 selected from:

(E)-2-(5-Chloro-2-thienyl)-N-(1-{4-[1-(dimethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)ethanesulfonamide;

(E)-2-(5-Chloro-2-thienyl)-N-(1-{2-fluoro-4-[1-(4-morpholinyl)ethyl]phenyl}-2-oxo-3-pyrrolidinyl)ethanesulfonamide;

30

(E)-2-(5-Chloro-2-thienyl)-N-[1-(2-fluoro-4-{1-[(2-hydroxyethyl)(methyl)amino]ethyl}phenyl)-2-oxo-3-pyrrolidinyl]ethanesulfonamide;

(E)-N-{1-[4-(1-Aminoethyl)-2-fluorophenyl]-2-oxo-3-pyrrolidinyl}-2-(5-chloro-2-thienyl)ethanesulfonamide;

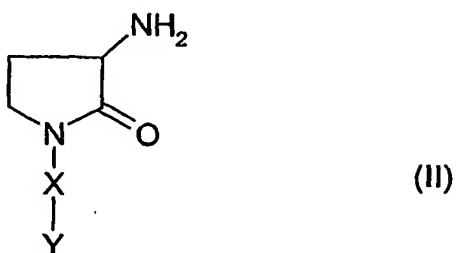
35 6-Chloro-N-(1-{4-[1-(dimethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-1-benzothiophene-2-sulfonamide;

(E)-2-(5-Chloro-2-thienyl)-N-((3S)-1-{4-[(1S)-1-(dimethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)ethanesulfonamide;

- 6-Chloro-*N*-((3*S*)-1-{4-[(1*S*)-1-(dimethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-2-naphthalenesulfonamide;
- 6-Chloro-*N*-((3*S*)-1-{4-[(1*S*)-1-(dimethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-1-benzothiophene-2-sulfonamide;
- 5 (E)-2-(5-Chloro-2-thienyl)-*N*-((3*S*)-1-{4-[(1*R*)-1-(dimethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)ethenesulfonamide;
- 6-Chloro-*N*-((3*S*)-1-{4-[(1*R*)-1-(dimethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-2-naphthalenesulfonamide;
- 6-Chloro-*N*-((3*S*)-1-{4-[(1*R*)-1-(dimethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-1-benzothiophene-2-sulfonamide;
- 10 (E)-2-(5-Chloro-2-thienyl)-*N*-((3*S*)-1-{4-[(1*R*)-1-(dimethylamino)ethyl]-2,6-difluorophenyl}-2-oxo-3-pyrrolidinyl)ethenesulfonamide;
- (E)-2-(5-Chloro-2-thienyl)-*N*-((3*S*)-1-{4-[(1*S*)-1-(dimethylamino)ethyl]-2,6-difluorophenyl}-2-oxo-3-pyrrolidinyl)ethenesulfonamide;
- 15 (E)-2-(5-Chloro-2-thienyl)-*N*-((3*S*)-1-{4-[1-(dimethylamino)propyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)ethenesulfonamide;
- (E)-2-(5-Chloro-2-thienyl)-*N*-((3*S*)-1-{4-[1-(dimethylamino)-2-methylpropyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)ethenesulfonamide;
- (E)-2-(5-Chloro-2-thienyl)-*N*-(1-{4-[1-(dimethylamino)-1-methylethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)ethenesulfonamide;
- 20 6-Chloro-*N*-(1-{4-[1-(dimethylamino)-1-methylethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-2-naphthalenesulfonamide;
- 6-Chloro-*N*-(1-{4-[1-(dimethylamino)-1-methylethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-1-benzothiophene-2-sulfonamide;
- 25 6-Chloro-*N*-(1-{4-[1-(dimethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-2-naphthalenesulfonamide;
- 6-Chloro-*N*-(1-{4-[1-(ethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-2-naphthalenesulfonamide;
- 6-Chloro-*N*-(1-{4-[1-(ethyl(methyl)amino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-2-naphthalenesulfonamide;
- 30 6-Chloro-*N*-(1-{2-fluoro-4-{1-[(1-methylethyl)amino]ethyl}phenyl}-2-oxo-3-pyrrolidinyl)-2-naphthalenesulfonamide;
- 6-Chloro-*N*-(1-{2-fluoro-4-{1-[methyl(1-methylethyl)amino]ethyl}phenyl}-2-oxo-3-pyrrolidinyl)-2-naphthalenesulfonamide;
- 35 *N*-(1-{4-[1-(1-Azetidinyl)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-6-chloro-2-naphthalenesulfonamide;

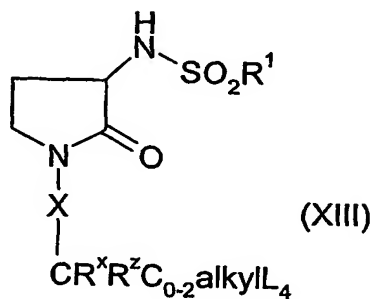
- 6-Chloro-*N*-(1-{2-fluoro-4-[1-(1-pyrrolidinyl)ethyl]phenyl}-2-oxo-3-pyrrolidinyl)-2-naphthalenesulfonamide;
- 6-Chloro-*N*-(1-{2-fluoro-4-[1-(1-piperidinyl)ethyl]phenyl}-2-oxo-3-pyrrolidinyl)-2-naphthalenesulfonamide;
- 5 5'-Chloro-*N*-((3*S*)-1-{4-[1-(dimethylamino)ethyl]-2-fluorophenyl}-2-oxo-3-pyrrolidinyl)-2,2'-bithiophene-5-sulfonamide;
- (*E*)-2-(5-Chloro-2-thienyl)-*N*-((3*S*)-1-{4-[(1*S*)-1-(dimethylamino)ethyl]phenyl}-2-oxo-3-pyrrolidinyl)ethenesulfonamide;
- (*E*)-2-(5-Chloro-2-thienyl)-*N*-((3*S*)-1-{4-[(1*R*)-1-(dimethylamino)ethyl]phenyl}-2-oxo-3-pyrrolidinyl)ethenesulfonamide;
- 10 6-Chloro-*N*-((3*S*)-1-{4-[(1*S*)-1-(dimethylamino)ethyl]phenyl}-2-oxo-3-pyrrolidinyl)-1-benzothiophene-2-sulfonamide;
- 6-Chloro-*N*-((3*S*)-1-{4-[(1*R*)-1-(dimethylamino)ethyl]phenyl}-2-oxo-3-pyrrolidinyl)-1-benzothiophene-2-sulfonamide;
- 15 (1*E*)-2-(5-Chloro-2-thienyl)-*N*-(1-{4-[1-(dimethylamino)ethyl]-2,6-difluorophenyl}-2-oxo-3-pyrrolidinyl)-1-propene-1-sulfonamide;
- 6-Chloro-*N*-(1-{4-[1-(dimethylamino)ethyl]-2,6-difluorophenyl}-2-oxo-3-pyrrolidinyl)-1-benzothiophene-2-sulfonamide;
- and/or pharmaceutically acceptable derivative thereof.
- 20
8. A compound according to any one of claims 1-7 and/or pharmaceutically acceptable derivative thereof for use in therapy.
9. A pharmaceutical composition comprising a compound according to any one of claims
- 25 1-7 and/or pharmaceutically acceptable derivative thereof together with at least one pharmaceutical carrier and/or excipient.
10. Use of a compound according to any one of claims 1-7 and/or pharmaceutically acceptable derivative thereof for the manufacture of a medicament for the treatment of a
- 30 patient suffering from a condition susceptible to amelioration by a Factor Xa inhibitor.
11. A method of treating a patient suffering from a condition susceptible to amelioration by a Factor Xa inhibitor comprising administering a therapeutically effective amount of a compound according to any one of claims 1-7 and/or pharmaceutically acceptable
- 35 derivative thereof.
12. A process for preparing a compound of formula (I) which comprises:

(a) reacting compounds of formula (II) or an acid addition salt thereof with compounds of formula (III) where V is a suitable leaving group:



OR:

(b) by reacting compounds of formula (XIII) with  $\text{HNR}^c\text{R}^d$ :



OR:

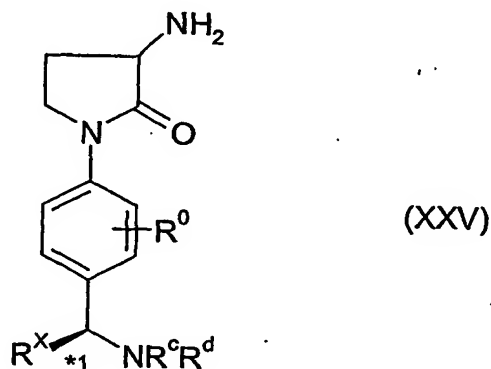
(c) by reacting compounds of formula (I) where  $\text{R}^2$  is hydrogen with compounds of formula (XVII):



wherein  $\text{R}^2$  is  $-\text{C}_{1-6}\text{alkyl}$ ,  $-\text{C}_{1-3}\text{alkylCONR}^a\text{R}^b$ ,  $-\text{C}_{1-3}\text{alkylCO}_2\text{C}_{1-4}\text{alkyl}$ , or  $-\text{CO}_2\text{C}_{1-4}\text{alkyl}$  and T is a suitable leaving group, optionally followed by removal of the alkyl protecting group where appropriate;

OR:

(d) by reacting a compound of formula (XXV) where X represents phenyl, Y represents  $\text{CH}(\text{R}^x)\text{NR}^c\text{R}^d$ ,  $\text{R}^c$  and  $\text{R}^d$  each represent the same  $\text{C}_{1-6}$ alkyl substituent and  $\text{R}^0$  represents 0-2 optional substituents on the phenyl ring selected from: halogen,  $-\text{C}_{1-4}$ alkyl,  $-\text{C}_{2-4}$ alkenyl,  $-\text{CN}$ ,  $-\text{CF}_3$ ,  $-\text{NR}^a\text{R}^b$ ,  $-\text{C}_{0-4}\text{alkylOR}^e$ ,  $-\text{C}(\text{O})\text{R}^f$  and  $\text{C}(\text{O})\text{NR}^a\text{R}^b$  and/or an acid addition salt thereof:

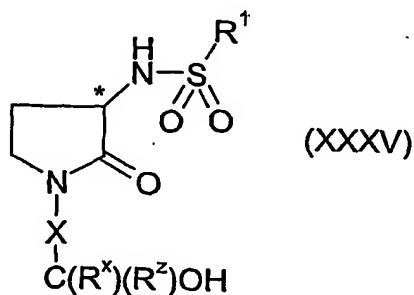


with a compound of formula (III) where V is a suitable leaving group:



OR:

(e) treatment of compounds of formula (XXXV) where Y represents  $-\text{C}(\text{R}^x)(\text{R}^z)\text{NR}^c\text{R}^d$  and  $\text{R}^x$  and  $\text{R}^z$  both represent  $\text{C}_{1-4}$ alkyl and  $\text{R}^2$  represents hydrogen:



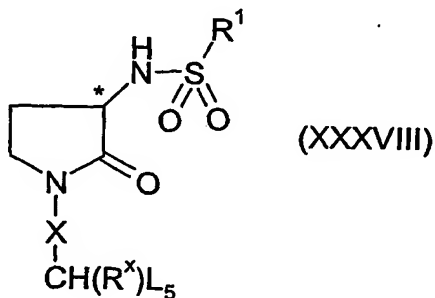
with hydrogen chloride in the presence of zinc chloride, followed by reaction with  $\text{HNR}^c\text{R}^d$ ;

OR:



(f) by reacting compounds of formula (XXXVIII) where Y represents  $-C(R^x)NR^cR^d$ ,  $R^x$  represents  $C_{1-4}$ alkyl and  $R^c$  and  $R^d$  independently represent hydrogen,  $C_{1-6}$ alkyl, or together with the N atom to which they are bonded form a 4-, 5-, 6- or 7- membered non-aromatic heterocyclic ring and  $L_5$  is a suitable leaving group:

5



with  $HNR^cR^d$ .